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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/092,210	03/06/2002	Iwao Katsuyama	KUP-D0201	8614

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BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER	
SOROUSH, LAYLA	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 12/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/092,210	KATSUYAMA, IWAO	
	Examiner	Art Unit	
	Layla Soroush	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 8/3/06.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 28-34 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 28-34 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The response filed August 3, 2006 presents remarks and arguments submitted to the office action mailed May 5, 2006 is acknowledged.

Applicant's arguments over the 35 U.S.C. 103 (a) rejection of claims 24-29, 32-36, over Nakagawa et al. (5, 142, 6457) in view of JP 07-133225 (JP '225) is not persuasive. Therefore, the rejection is herewith maintained.

Applicant's arguments over the 35 U.S.C. 103 (a) rejection of claims 30-31, 37-38 over Nakagawa et al. (5, 142, 6457) in view of JP 07-133225 (JP '225) and Kitagaw (Japanese Journal of Pharmacology) is not persuasive. Therefore, the rejection is herewith maintained.

The rejections are restated below for Applicant's convenience:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 28-29, 32-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nakagawa et al. (5, 142, 6457) in view of JP 07-133225 (JP '225).

The instant claims are directed to methods for evaluating the action of a drug against ciliary muscles for evaluating the effect of the drug against asthenopia comprising the steps of inducing contraction of ciliary muscles and contacting ciliary muscles with a medicine and assessing the decrease in ciliary muscle tension.

Nakagawa teaches an in vitro method of measuring effects of pharmaceutical solutions against biological specimen including smooth muscles and the like (see abstract; col 2, line 46-col 3, line 25). The Magnus Apparatus of Nakagawa contains a chamber wherein a muscle specimen is immersed into a solution from one end and is attached to a transducer from the other end for detection of the tensile force of the specimen (see figure 1, numeral 1-5, 10; col 5, line 60-col 6, line 14; col 6, lines 40-67). The chamber also known as magnus tube can contain a solution of tensile stimulant or the pharmaceutical agent of choice to be tested. (see figure 1, col 3, line 50-col 4, line 67).

Nakagawa fails to explicitly employ ciliary muscles in his magnus apparatus or assess the activity of drugs against asthenopia. JP '225 describes methods of performing a pharmacological test to assess the effects of a drug on ciliary muscle contraction for treatment of asthenopia. (Abstract).

The methods of JP '225 teaches all elemental steps of the instant claims. The method in JP '225 comprise extracting the ciliary muscles of a cow eyeball which meets the instant step of enucleating ciliary muscles of a non-human mammal. (see para 0022- 0023). The method of JP '225 also comprises hanging the ciliary muscle and placing it in a Magnus apparatus (tubing) and applying a compound of interest (compound A) to the hung muscle and then determining the contraction strength of the ciliary muscles (see para 0023). The ciliary muscles in JP '225 are first contracted or pretreated with compound A to induce astoponia. This step in JP '225 meets the limitation of inducing contraction of ciliary muscles. The step of adding KCl in JP '225

meets the instant step of contacting a "medicine" to the contracted muscles. JP '225 describes that the rate of decrease in tension was about 22.9% which meets the limitations of the instant claims. Examiner points out in the process claims, the intended use does not impart patentability over the prior art absent a manipulative difference Thus, all process steps of the instant claims are met.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of invention to assess the activity of suitable drugs such as Compound A in JP '225 against other chemical stimulants in the Magnus Apparatus of Nakagawa, because as suggested by both Nakagawa and JP'225, such device and process steps provide in vitro assessment of the efficacy of drugs on contracted ciliary muscles. Further, absent a showing of unexpected results, it would have been obvious to one of ordinary skill in the art at the time of invention to optimize the tension degree of muscle tension to best mimic the in vivo tension of asthoponic ciliary muscles, such as acetylcholine, as described by Kitagaw, or directelectrical stimulation, as described by Yoshikawa.

One of ordinary skill in the art would have had a reasonable expectation of success in achieving meaningful clinical data by predicting the degree of contraction of ciliary muscles against other known stimulants. Further, assessing the degree of contraction decrease is a function of the doses of an agonist or antagonist drug employed and is achieved by routine experimentation.

Claims 30-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nakagawa et al US Patent 5,142,647 in view of JP 07-133225 ("JP '225") as applied to

claims 28-29, 32-34 and further in view of JP '225 in view of Kitagaw. (Japanese Journal of Pharmacology, 1989, Vol 49, suppl, pp. 281).

The teachings of Nakagawa and JP '225 are described above. Their combined teachings fails to employ acetylcholine as the stimulatory agent for contracting ciliary muscles prior to their exposure to the drug of interest for asthenopia. Kitagaw teaches acetylcholine-induced contraction of smooth muscles and measuring the degree of contraction by automated and manual Magnus apparatus. Accordingly, it would have been obvious to one of ordinary skill in the art at the time of invention to further use chemical stimulatanst such as acetylcholine and assess the activity of Compound A in JP '225 against other chemical stimulants.

One of ordinary skill in the art would have had a reasonable expectation of success in achieving meaningful clinical data by predicting the degree of contraction of ciliary muscles against other known stimulants. Further, assessing the degree of contraction decrease is a function of the doses of an agonist or antagonist drug employed and is achieved by routine experimentation.

Response to Arguments

Applicant's arguments filed August 3, 2006 have been fully considered. The response to the arguments is as discussed below:

The method of using the same ciliary muscle repeatedly to evaluate multiple medicines and evaluating the decrease in tension of the muscle contraction by the medicine is within the realms of a skilled artisan. The process of repeating, (part (b) of instant claim 28), the same method as taught in the prior art is deemed obvious by a

skilled artisan. Further, a skilled artisan would obviously wash the ciliary muscle between use of various drugs. Additionally, applicants argue that the evaluation of a medicine is used on a normal muscle contraction "as is" whereas the invention herein evaluates the medicine on a muscular contraction decreases to 50-20%; Examiner respectfully reiterates: " it would have been obvious to one of ordinary skill in the art at the time of invention to assess the activity of suitable drugs such as Compound A in JP '225 against other chemical stimulants in the Magnus Apparatus of Nakagawa, because as suggested by both Nakagawa and JP'225, such device and process steps provide in vitro assessment of the efficacy of drugs on contracted ciliary muscles. Further, absent a showing of unexpected results, it would have been obvious to one of ordinary skill in the art at the time of invention to optimize the tension degree of muscle tension to best mimic the in vivo tension of asthoponic ciliary muscles, such as acetylcholine, as described by Kitagaw, or directelectrical stimulation, as described by Yoshikawa.

One of ordinary skill in the art would have had a reasonable expectation of success in achieving meaningful clinical data by predicting the degree of contraction of ciliary muscles against other known stimulants. Further, assessing the degree of contraction decrease is a function of the doses of an agonist or antagonist drug employed and is achieved by routine experimentation."

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the

references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the Kitawag reference is solely incorporated to show that acetylcholine has previously been used in evaluating smooth muscle cells. Therefore, it would have been obvious to a skilled artisan to incorporate this stimulant in the invention of JP 07-133225.

The arguments are not persuasive and the rejection is made **FINAL**.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

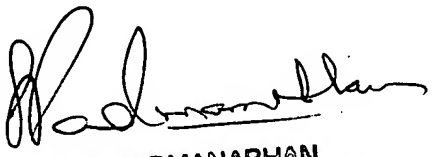
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Layla Soroush whose telephone number is (571)272-5008. The examiner can normally be reached on Monday through Friday from 8:30 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER